

REMARKS

Reconsideration of the application as amended above is respectfully requested.

Claims 1-13 were pending. Claims 8 - 12 were withdrawn from consideration by the Examiner. Claims 1 – 6 and 13 are rejected. Claim 7 is objected to. Claims 1 - 7 and 13 have been amended. Currently, Claims 1 - 7 and 13 are pending in the present application.

Withdrawn Claims 8 - 12 have been cancelled to comply with the Restriction Requirement, without prejudice to pursuing the cancelled subject matter in a divisional application.

Claim 1 has been amended to:

- 1) replace the definition of R1 with the definition of R1 from page 3, lines 22-29 of the specification, this definition is further amended to delete the rings formed with R1 and R2 as required by the Restriction Requirement;
- 2) replace the definition of R2 with the definition of R2 from page 6, lines 24-29 of the specification, this definition is further amended to delete the rings formed by R1 and R2 as required by the Restriction Requirement;
- 3) define R3 as hydrogen as required by the Restriction Requirement;
- 4) replace the definition of R5 and R6 with the definition of R5 and R6 from original Claim 4;
- 5) replace the definition of R8 with the definition of R8 from original Claim 4;
- 6) replace the definitions of Ar1 and Ar2 with the definitions of Ar1 and Ar2 from original Claim 2.

Claim 2 has been amended to delete the definitions of R3, Ar1 and Ar2.

Claim 3 has been amended to delete the definition of R2.

Claim 4 has been amended to depend from Claim 2 instead of canceled Claim 3, and to delete the definitions of R5, R6 and R8.

Claim 5 has been amended to delete the definition of the 4-7 membered ring formed by the R1 and R2 substituents as required by the Examiner's Restriction Requirement. This subject matter has been deleted from Claim 5 without prejudice to pursuing the deleted subject matter in a divisional application.

Claim 6 has been amended to depend from Claim 1 instead of Claim 2, and to refer to the definitions of R1, R2 and R4 as defined in Claim 1 instead of Claim 2.

Claim 7 has been amended to delete the specific compounds in which R1 and R2 together form a ring, as required by the Examiner's Restriction Requirement. This subject matter has been deleted without prejudice to pursuing the canceled subject matter in a divisional application.

These amendments do not add new matter to the present application.

CLAIM REJECTION UNDER 35 USC 112.

FIRST PARAGRAPH

The Examiner stated that Claims 1-7 and 13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while enabling for some substituents, such as R1 is $-\text{C}(\text{O})\text{CH}_3$, alkyl, halogen; R2 is alkyl or NR^5R^6 and R5 and R6 are H, alkyl, CO_2Rc and some other variables as given in the table; R4 is alkyl or an alkyl aryl, does not reasonably provide enablement for all the various substituents such as the heteroaryl, cycloheteroalkyl, cycloalkyl and so on. The Examiner further stated that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicants have amended Claim 1 by replacing the definition of R1 in Claim 1 with the definition of R1 from page 3, lines 22-29 of the specification. Support for the following R1 substituents is found in the Examples cited below:

R¹ is selected from:

- (1) hydrogen – Examples 4 and 5;
- (2) halogen – Examples 61-71;
- (3) $-\text{C}_{1-4}\text{alkyl}$ – Examples 3 (OH substituted), Example 60 (OCH₃ substituted), Examples 38-58 (alkyl);
- (4) $-\text{CN}$ – Examples 98 and 99;
- (5) $-\text{COR}^7$ – Examples 1, 7, 8 ($-\text{C}(\text{O})\text{alkyl}$), Examples 91-94 ($-\text{CO}_2\text{alkyl}$), Example 95 ($-\text{C}(\text{O})\text{NH}_2$), and Examples 72-77 and 96 ($-\text{C}(\text{O})\text{N}(\text{CH}_3)_2$);
- (6) $-\text{OR}^d$ – Examples 80-82, 86 and 87 (OCH₃);
- (7) $-\text{NR}^5\text{R}^6$ – Examples 72-77 ($\text{N}(\text{CH}_3)_2$); and
- (8) cycloheteroalkyl – Examples 78 and 79 (piperidine).

Applicants have amended Claim 1 by replacing the definition of R2 in Claim 1 with the definition of R2 from page 6, lines 24-29 and deleting the rings formed using R1 and R2. Support for the following R2 substituents is found in the examples cited below:

R² is selected from:

- 1) -NR⁵R⁶, - Examples 1, 2, 9, 10, 11, 12, 28, 32, 34, 33, 46, 48, 50, 51, 52 and 89; and
- 2) C₁₋₆alkyl.

Applicants have amended Claim 1 to define R3 as hydrogen as required by the Examiner's Restriction Requirement.

Applicants have not amended the R4 substituent of Claim 1 because there is support for the following R4 substituents is found in the Examples cited below:

R⁴ is selected from:

- (1) hydrogen - Example 30; and
- (2) -CH₂-R⁸ - Examples 1-5 (CH₃), Examples 23, 28-29 (benzyl), Example 15 (CH₂-cyclopropyl), Example 19 (CH₂-furan), Examples 20, 21 and 24 (CH₂-pyridine), Example 22 (CH₂CH₂)OC(O)CH₃), Example 18 (CH₂-alkoxy) and Example 31 (CH₂CH₂OH).

Applicants have amended Claim 1 by replacing the definitions of R5 and R6 in Claim 1 with the definitions of R5 and R6 from original Claim 4. Support for the following R5 and R6 substituents is found in the Examples cited below:

R⁵ is selected from:

- (1) hydrogen – Examples 1, 2, 3, 4, 7, 38 and 39;
- (2) C₁₋₆alkyl – Example 10;
- (3) trifluoromethyl, and
- (4) methylcarbonyl- Examples 28, 29 and 69.

R⁶ is each selected from:

- (1) hydrogen – Examples 2 and 4;
- (2) C₁₋₆alkyl – Examples 10 and 89;

- (3) phenyl,
- (4) benzyl – Example 9;
- (5) trifluoromethyl,
- (6) $-C(O)-R^C$ – Examples 1,3, 7, 11, 12, 28, 29, 33, 34, 38, 39, 46, 48, 50, 51, 52 and 69,
- (7) $-CO_2R^C$, and
- (8) $-S(O)_2CH_3$ – Example 32; and

or R^5 and R^6 together form $=CH-N(CH_3)_2$. – Examples 83 – 86.

Applicants submit that one of skill in the art would know how to prepare the compounds of the present invention based on the syntheses provided in Schemes 1-11 and Examples 1-91 in the specification, and the known chemical syntheses in the art. Therefore, even the non-exemplified compounds claimed in the present invention are enabled. Further, employing the CB-1 binding assay described in Biological Example 1 and the CB-1 functional assay in Biological Example 2, one of ordinary skill in the art would recognize that the compounds of the present application are cannabinoid-1 receptor modulators useful for treating diseases responsive to modulation of the cannabinoid-1 receptor, such as obesity.

Finally, Applicants submit that the compounds referred to and synthesized in Scheme 1.6 of the Dorwald reference are structurally distinct from the compounds of the present invention. In Scheme 1.6, Dorwald treats a polycyclic dicyclopentyl cyclobutylmethyl compound with AIBN in the presence of tributyltin to form a radical in the compound, which then results in the rearrangement of the compound to a more stable molecular structure due to the radical's unpaired free electron (represented by the dot in the scheme).

The compounds in Scheme 1.6 of Dorwald are subject to synthetic conditions that are not employed to synthesize the compounds of the present invention. The compounds of the present invention are not synthesized by generating free radicals using AIBN or via radical rearrangement reactions, such as the one shown in Dorwald. Further, as Dorwald quotes in the conclusion "the outcome of organic reactions is highly dependent on all structural features of a given starting material...". Dorwald's starting material is a polycyclic dicyclopentyl cyclobutylmethyl compound, whereas the present invention relates to substituted naphthyridinone compounds. The side reactions shown in Scheme 1.6 of Dorwald are the result of a rearrangement of the radical of the cyclopentene spiro cyclohexanone compound. Such side reactions would not be encountered in the syntheses of the compounds of the present invention because of the differing synthetic methods and starting materials employed to synthesize the compounds of the present invention.

Applicants submit that the compounds of the present invention can be prepared via the synthetic methods disclosed in the present application, and that the chemistry illustrated in Scheme 1.6 of Dorwald is not related to the chemistry used to prepare the compounds of the present invention.

In view of the above amendments and arguments, Applicants submit that Claims 1-7 and 13 are enabled. Applicants respectfully request that the rejection of Claims 1-7 and 13 under 35 USC § 112 first paragraph be withdrawn.

CLAIM OBJECTION

The Examiner stated that Claim 7 is objected to as containing non-elected subject matter.

Applicants have amended Claim 7 to delete compounds in which R1 and R2 together form a ring, as required by the Examiner's Restriction Requirement. Applicants have amended Claim 7 without prejudice to pursuing the canceled subject matter in a divisional application.

Applicants submit that based on the amendments to Claim 7, Claim 7 is allowable. In view of the above amendments, Applicants respectfully request that the objection to Claims 7 be withdrawn.

Applicants believe that all of the rejections and objections have been overcome and therefore earnestly solicit a Notice of Allowance.

Respectfully submitted,

By: /Baerbel R. Brown, Reg. # 47449/

Baerbel R. Brown, Reg. No. 47,449
Patent Attorney for Applicants

MERCK & CO., Inc.
P.O. Box 2000
Rahway, New Jersey 07065
Tel.: (732)594-0672

September 3, 2009